REMARKS

This is in response to the Office Action mailed June 29, 2006. Claims 1-36 are currently pending and rejected by the instant Office Action. Applicants present certain arguments herein and believe these arguments address the current grounds for rejection. Reconsideration and allowance are respectfully requested in view of the foregoing amendments and the following representations.

Claims 1-36 have been rejected under 35 USC 103(a) as being obvious over US Patent 2,956,062 (hereinafter the '062 patent) in view of US Patent 4,353,922 (hereinafter the '922 patent).

The Office action states the '062 disclosure is deficient in that is does not show the quaternary ammonium group nor does it teach the compound of the subject application for treating asthma. The Office action attempts to combine '062 with '922 to teach a quaternary ammonium group on an asthma treating molecule, but the '922 is equally deficient because it does not teach the pyrrolidinium compound of the subject invention.

The Examiner states that there are only slight differences between the compound disclosed in the '062 patent and the present application, and that the '062 teaches that the diastereoisomers are similarly effective and useful in the invention as the racemic forms. This is not a correct reading of the '062 disclosure. The Office Action cites col. 1,

lines 62—72. But this efficacy and usefulness is a misinterpretation of the disclosure. The '062 "…these diasteroisomers, together with their optically active forms are included within the scope of the present invention". There is no teaching or suggestion anywhere in the '062 disclosure that the efficacy of single isomers might differ from that of the racemic forms.

Regarding the '922 disclosure, the Office Action states that "…the only difference being the compound of '922 is having a bridged bicycle quaternary amino group, instead of pyrrolidonium compound." This compound is an acetylcholine antagonist that is useful in treating asthma, but even if one assumes that you can incorporate the pyrrolldonium moiety, this does not lead to the conclusion that the so changed compound is useful as acetylcholine antagonist. Because, it is well known to those skilled in the chemical arts that even a small change of a functional group in a complex molecule may lead to unexpected effects. The resulting substance may have affinity or lack thereof to certain receptors due to the change in the reactivity of the molecule (e.g. stencal effects). Moreover the '922 disclosure does not teach or suggest any information about different efficacy for specific isomers as set forth in the subject application.

Applicant asserts it is not obvious to a person skilled in the art to combine the two documents cited by the Office Action and arrive at the invention of the subject application because the subject application is focused on certain enantiomers with much higher binding activity than the racemic forms. The subject application does not claim the treatment of respiratory diseases using 3-[(cyclohexylhydroxyphenylacetyl0)oxy]-1 ,1 dimethylpyrrolidonium but only pure enantiomers thereof, namely the 3R, 2'R and 3S, 2'R enantiomers. The Office Action does not take into account the great differences of the efficacy of the enantiomers.

These differences are a main novelty of the present invention.

Another difference is high dissociation half-life of the claimed isomer at the MS receptor subtype, and in particular, the high half-life at the M3 receptor subtype associated with the much lower half-life at the M2 receptor subtype. This kinetic difference gives rise to the selectivity that reduces the number of side effects during treatment. The mechanism underlying the invention is not simply an increased affinity of certain isomers but the combination of effects as stated above. Applicant asserts this was not obvious to a person skilled in the art, and could not be obvious from either the '062 or '962 disclosures taken alone or in combination.

The subject application further provides data for the enantiomerically pure substances with the same configurations at the chiral centres but with cyclopentyl as R1 instead of cyclohexyl in the disclosure of the subject application (see generally Ex 1-2, pages 25-30; Ex 4, p 31-32; Ex 9-10, pp. 38-40).

The Office Action concludes with the assessment that "absent some difference in kind between the various isomers, the skilled artisan would have seen each isomer as prima facie obvious."

Applicant respectfully asserts the difference in kind has been established herein, and further asserts that the Office recognize established case law which characterized most chemical reactions and physiological activity as "unpredictable" *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). It is a well-established tenet that the unpredictable nature of the chemical arts requires a higher standard to show obviousness.

In view of the failure of the '062 patent alone, or in combination with the '920 patent to provide the requisite

teaching or suggestion, and in further view of the distinctions presented herein between the subject application and the cited references, applicant asserts an obviousness rejection cannot properly stand. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-36 under 35 USC 103(a).

Based upon the representations presented herein, Applicant respectfully asserts the application is in condition for allowance. If the Examiner believes there any issues that have not been resolved the Examiner is invited to call the undersigned representative who is attorney of record in this case.

The issuance of a Notice of Allowance is requested.

/Werner H. Stemer/

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